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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
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| 09/926,163 | 12/21/2001 | Takashi Shibata | 213930US0PCT | 7098 |

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| EXAMINER | |
|---|---|
| PAK, YONG D | |

| ART UNIT | PAPER NUMBER |
|---|---|
| 1652 | 14 |

DATE MAILED: 06/02/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 09/926,163 | SHIBATA ET AL. | |
| | Examin r | Art Unit | |
| | Yong Pak | 1652 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *28 April 2003* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *1-48* is/are pending in the application.

4a) Of the above claim(s) *6-9 and 11-48* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-5 and 10* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

**Priority under 35 U.S.C. §§ 119 and 120**

13)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

**Attachment(s)**

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *5,8&12* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

## DETAILED ACTION

### *Election/Restrictions*

Applicant's election with traverse of Group I (claims 1-5 and 10) in Paper No. 13 is acknowledged. The traversal is on the ground(s) that the Office has not provided adequate reasons and/or examples to support a conclusion of patentable distinctness between the identified groups. Applicants argue that the office has not applied the same standard of unity of invention as the IPEA. This is not found persuasive because the office is not bound by the actions taken by the IPEA.

Applicants argue that the Office has simply stated a conclusion and has not supplied reasons or examples in support to conclude that Groups I-V are different. This is not found persuasive because the Restriction Requirement states that the technical feature linking the inventions of Groups I-V does not constitute a special technical feature as defined by PCT Rule 13.2, as it does not define a contribution over the prior art. Hoshino et al. (from PTO-892) teach a sorbitol dehydrogenase that can be construed as a polypeptide comprising an amino acid sequence of SEQ ID NO:I wherein one or more amino acid residues have been deleted, substituted, inserted, added or modified.

Applicants also argue that multiple products and processes can be claimed in one application and submit that the requirement for restriction be withdrawn. This is not found persuasive because the inventions of Groups I-V does not constitute a special technical feature as defined by PCT Rule 13.2, as it does not define a contribution over the prior art. Therefore, only Group I will be examined.

Applicants also argue that a search of all the claims would not impose a serious burden on the Office, since the ISA has searched all the claims together. This is not found persuasive because as noted above, the Office is not bound by actions taken by the ISA. Further, because of the recognized divergent subject matter of Groups II-V from Group I, an unduly extensive and burdensome search is required for Groups II-V that is not necessary for Group I.

The requirement is still deemed proper and is therefore made FINAL.

Claims 6-9 and 11-48 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in Paper No. 13.

***Claim Objections***

Claim 10 is objected to as being dependent upon a non-elected base claim, and should be rewritten in independent form including all of the limitations of the base claim and any intervening claims.

Claim 10 has been interpreted to include all the limitations of its base claim and any intervening claims.

***Claim Rejections - 35 USC § 101***

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 1-5 and 10 are rejected under 35 U.S.C. 101 because the claimed invention is directed to a non-statutory subject matter. Claims 14-15 read on a product of nature. This rejection can be overcome by amending claims 14-15 as "an isolated peptide", for example.

***Claim Rejections - 35 USC § 112***

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1, 3-5 and 10 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claim 1 is drawn to sorbitol dehydrogenase with limitations to its physicochemical properties and claim 10 is drawn to sorbitol dehydrogenase encoded by DNA that hybridizes to fragments of SEQ ID NO:2. Therefore, these claims are drawn to a genus of sorbitol dehydrogenase, with any structure and from any source. The specification only teaches one sorbitol dehydrogenase from *Gluconobacter oxydans* G624 of SEQ ID NO:1. Only one representatives of this wide genus containing sorbitol dehydrogenase

from any source and structure is not enough to describe the whole genus. Although claim 4 limits the genus to the Gluconobacter family and claim 3 to homologous sorbitol dehydrogenase to SEQ ID NO:1, there is no evidence on the record of the relationship between the structure of a *G. oxydans* G624 sorbitol dehydrogenase and the structure of a sorbitol dehydrogenase from another source. Further, art teaches that in two strains of genus Gluconobacter, G. suboxydans subsp. var IFO 3254 and G. suboxydans ATCC 621, the occurrence of two different D-sorbitol dehydrogenases in the membrane fraction has been indicated (Adachi et al., page 1589). Therefore, it is unpredictable whether the sorbitol dehydrogenase belonging to the genus of Gluconobacter are dehydrogenases with the same or different substrate specificity as the sorbitol dehydrogenase of SEQ ID NO:1. Therefore, the specification fails to describe the wide genus of sorbitol dehydrogenase having the physicochemical properties of claim 1.

Claim 5 is drawn to a sorbitol dehydrogenase from any source wherein one or more amino acids of SEQ ID NO:1 are modified by deletion, addition, insertion, or substitution. Since there is no limit to structure or source of the polypeptides, the claim encompasses a genus of molecules described by the function of sorbitol dehydrogenase activity. The single species sorbitol dehydrogenase of SEQ ID NO:1 is insufficient to describe the whole genus containing a vast number and combinations of amino acid deletions, insertions, additions, or substitutions. The specification fails to place limitations on the sorbitol dehydrogenase structure or disclose which amino acid(s) of SEQ ID NO:1 can be safely modified and still impart (R)-2-octanol dehydrogenase activity. Therefore, the specification fails to describe other

representative species from other sources or by identifying characteristics or structural properties other than the functionality of being a sorbitol dehydrogenase.

Given this lack of the description of the representative species encompassed by the genus of the claims, the specification fails to sufficiently describe the claimed invention in such full, clear, concise, and exact terms that a skilled artisan would recognize that applicants were in possession of the inventions of claims 1, 3-5 and 10.

Claims 1, 3-5 and 10 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a sorbitol dehydrogenase of SEQ ID NO:1, does not reasonably provide enablement for sorbitol dehydrogenase of unknown structure. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make the invention commensurate in scope with these claims.

Factors to be considered in determining whether undue experimentation is required, are summarized in In re Wands 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988). They include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims.

Despite knowledge in the art for the isolation of amino acids, the specification fails to provide guidance regarding how to isolate other sorbitol dehydrogenase whose

sequence is different to SEQ ID NO:1. Therefore, the breadth of these claims is much larger than the scope enable by the specification.

The predictability as to the level of conservation between the disclosed sequences and those of other sorbitol dehydrogenase different from SEQ ID NO:2 is extremely complex. While recombinant techniques are available, it is not routine in the art to screen large numbers of amino acids where the expectation of obtaining similar sequences is unpredictable. The amino acid sequence determines the structural and functional properties of an enzyme. Knowledge of which sequences can be altered or removed and still result in similar protein activity is well outside the realm of routine experimentation.

Regarding claim 5, the specification, as discussed above which places no limit to the source or structure of sorbitol dehydrogenase, does not support the broad scope of the claims because the specification does **not** establish: (A) regions of the protein structure which may be modified without effecting sorbitol dehydrogenase activity; (B) the general tolerance to modification and extent of such tolerance; (C) a rational and predictable scheme for modifying any residues with an expectation of obtaining the desired biological function; and (D) the specification provides insufficient guidance as to which of the essentially infinite possible choices is likely to be successful.

Since the amino acid sequence of a protein determines its structural and functional properties, predictability of which changes can be tolerated in a protein's amino acid sequence and obtain the desired activity requires a knowledge of and guidance with regard to which amino acids in the protein's sequence, if any, are tolerant

of modification and which are conserved (i.e. expectedly intolerant to modification), and detailed knowledge of the ways in which the proteins' structure relates to its function.

While recombinant and mutagenesis techniques are known, it is not routine in the art to screen for substitutions, deletions, insertions/additions or multiple modifications, as encompassed by the instant claims. Also, the positions within a protein's sequence where amino acid modifications can be made with a reasonable expectation of success in obtaining the desired activity/utility are limited in any protein and the result of such modifications is unpredictable. In addition, one skilled in the art would expect any tolerance to modification for a given protein to diminish with each further and additional modification, e.g. multiple substitutions.

Therefore, one of ordinary skill would require guidance in order to make polypeptides having (sorbitol dehydrogenase activity with structures different from SEQ ID NO:1 in a manner reasonable correlated with the scope of the claims. Without such guidance, the experimentation left to those skilled in the art is undue.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1, 3 and 10 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

In claim 3, it is unclear if the claim is referring to spliced variants, isoforms or homologous proteins of the sorbitol dehydrogenase of SEQ ID NO:1. This claim has been interpreted to include all the said definitions.

In claim 10, the exact hybridization condition is unclear. Different nucleic acids hybridize to a DNA sequence under different conditions. Therefore, the scope of proteins encoded by the DNA molecules in claim 10 is unclear.

### *Claim Rejections - 35 USC § 102*

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 3-5 and 10 are rejected under 35 U.S.C. 102(b) as being anticipated by Adachi et al.

Adachi et al. (form PTO-1449) teach a sorbitol dehydrogenase from Gluconobacter suboxydans (abstract and page 1590). This sorbitol dehydrogenase can be construed as the amino acid sequence of SEQ ID NO:1 wherein one or more amino acids are modified by deletion, substitution, insertion or addition. The DNA encoding the dehydrogenase of Adachi et al. is capable of hybridizing to the fragments or partial sequences of the DNA of SEQ ID NO:1. Therefore, the teachings of Adachi et al. anticipate claims 3-5 and 10.

Applicant cannot rely upon the foreign priority papers to overcome this rejection because a translation of said papers has not been made of record in accordance with 37 CFR 1.55. See MPEP § 201.15.

Claims 3-5 and 10 are rejected under 35 U.S.C. 102(b) as being anticipated by Hoshino et al.

Hoshino et al. teach a sorbitol dehydrogenase from the genus of Gluconobacter (Column 2 through 11 and claims 1-3). This sorbitol dehydrogenase can be construed as the amino acid sequence of SEQ ID NO:1 wherein one or more amino acids are modified by deletion, substitution, insertion or addition. The DNA encoding the dehydrogenase of Hoshino et al. is capable of hybridizing to the fragments or partial sequences of the DNA of SEQ ID NO:1. Therefore, the teachings of Hoshino et al. anticipate claims 3-5 and 10.

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Yong Pak whose telephone number is 703-308-9363. The examiner can normally be reached on 6:30 A.M. to 3:30 P.M weekdays.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathapu Achutamurthy can be reached on 703-308-3804. The fax phone numbers for the organization where this application or proceeding is assigned are 703-872-9306 for regular communications and 703-872-9307 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

Yong Pak
Patent Examiner

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